MT-ND4L gene

mitochondrially encoded NADH:ubiquinone oxidoreductase core subunit 4L

Normal Function

The *MT-ND4L* gene provides instructions for making a protein called NADH dehydrogenase 4L. This protein is part of a large enzyme complex known as complex I, which is active in mitochondria. Mitochondria are structures within cells that convert the energy from food into a form that cells can use. These cellular structures produce energy through a process called oxidative phosphorylation, which uses oxygen and simple sugars to create adenosine triphosphate (ATP), the cell's main energy source.

Complex I is one of several enzyme complexes necessary for oxidative phosphorylation. Within mitochondria, these complexes are embedded in a tightly folded, specialized membrane called the inner mitochondrial membrane. During oxidative phosphorylation, mitochondrial enzyme complexes carry out chemical reactions that drive the production of ATP. Specifically, they create an unequal electrical charge on either side of the inner mitochondrial membrane through a step-by-step transfer of negatively charged particles called electrons. This difference in electrical charge provides the energy for ATP production.

Complex I is responsible for the first step in the electron transport process, the transfer of electrons from a molecule called NADH to another molecule called ubiquinone. Electrons are then passed from ubiquinone through several other enzyme complexes to provide energy for the generation of ATP.

Health Conditions Related to Genetic Changes

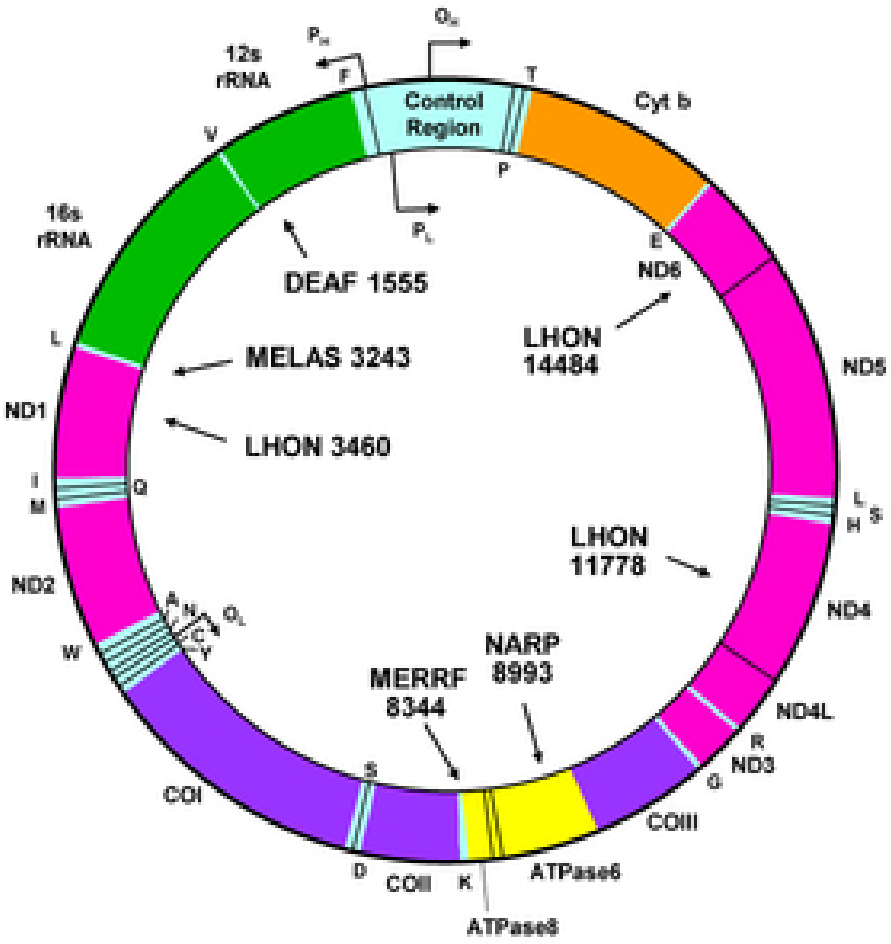
Leber hereditary optic neuropathy

A mutation in the *MT-ND4L* gene has been identified in several families with Leber hereditary optic neuropathy. This mutation, which can be written as T10663C or Val65Ala, changes a single protein building block (amino acid) in the NADH dehydrogenase 4L protein. Specifically, it replaces the amino acid valine with the amino acid alanine at protein position 65.

Researchers have not determined how a mutation in the *MT-ND4L* gene can lead to the vision loss characteristic of Leber hereditary optic neuropathy. This genetic change appears to disrupt the normal activity of complex I in the mitochondrial inner membrane, which may affect the production of ATP. It remains unclear, however, why the effects of this mutation are limited to the nerve that relays visual information from the eye to the brain (the optic nerve). Additional genetic and environmental factors probably contribute to the features of Leber hereditary optic neuropathy.

Chromosomal Location

Molecular Location: base pairs 10,470 to 10,766 on mitochondrial DNA (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Other Names for This Gene

- Complex I, subunit ND4L
- mitochondrially encoded NADH 4L
- mitochondrially encoded NADH dehydrogenase 4L
- MTND4L

- NADH dehydrogenase 4L
- NADH dehydrogenase subunit 4L
- NADH-ubiquinone oxidoreductase chain 4L
- NADH-ubiquinone oxidoreductase, subunit ND4L
- NADH4L
- ND4L
- NU4LM_HUMAN

Additional Information & Resources

Educational Resources

- Mayo Clinic Mitochondrial Disease Biobank
  http://www.mayo.edu/research/centers-programs/mitochondrial-disease-biobank/overview
- Oxidative Phosphorylation (Biochemistry, Fifth Edition, 2002)
  https://www.ncbi.nlm.nih.gov/books/NBK21208/
- The Neuromuscular Disease Center at Washington University: Complex I
  http://neuromuscular.wustl.edu/pathol/diagrams/mito.htm#complexI

GeneReviews

- Leber Hereditary Optic Neuropathy
  https://www.ncbi.nlm.nih.gov/books/NBK1174
- Mitochondrial Disorders Overview
  https://www.ncbi.nlm.nih.gov/books/NBK1224

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28MT-ND4L%5BTIAB%5D%29+OR+%28mitochondrially+encoded+NADH+4L%5BTIAB%5D%29%29+OR+%28%28MTND4L%5BTIAB%5D%29+OR+%28NADH+dehydrogenase+subunit+4L%5BTIAB%5D%29+OR+%28Complex+I,+subunit+ND4L%5BTIAB%5D%29+OR+%28NADH+dehydrogenase+4L%5BTIAB%5D%29+OR+%28NADH-ubiquinone+oxidoreductase+chain+4L%5BTIAB%5D%29+OR+%28NADH-ubiquinone+oxidoreductase,+subunit+ND4L%5BTIAB%5D%29+OR+%28NADH4L%5BTIAB%5D%29+OR+%28ND4L%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

OMIM

- COMPLEX I, SUBUNIT ND4L
  http://omim.org/entry/516004

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_ND4L.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=MT-ND4L%5Bgene%5D
- HGNC Gene Family: NADH:ubiquinone oxidoreductase core subunits
  http://www.genenames.org/cgi-bin/genefamilies/set/1149
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=7460
- Mitomap: Leber Hereditary Optic Neuropathy Disease Mutation Database
  http://www.mitomap.org/MITOMAP/MutationsLHON
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/4539
- UniProt
  http://www.uniprot.org/uniprot/P03901

Sources for This Summary

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  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/11935318
- GeneReview: Leber Hereditary Optic Neuropathy
  https://www.ncbi.nlm.nih.gov/books/NBK1174
- Mitchell AL, Elson JL, Howell N, Taylor RW, Turnbull DM. Sequence variation in mitochondrial complex I genes: mutation or polymorphism? J Med Genet. 2006 Feb;43(2):175-9. Epub 2005 Jun 21.
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Reviewed: August 2006
Published: March 21, 2017

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services